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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,726	06/27/2003	Anthony J. Kinney	BB1113USDIV	8251

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LEGAL PATENT RECORDS CENTER
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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 12/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/607,726	KINNEY ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-29* is/are pending in the application.

4a) Of the above claim(s) *29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 17-29 are pending.

2. Applicant's election without traverse of Group I, claims 1-9, including SEQ ID NO:6 in the reply filed on 10/25/2005 is acknowledged.

Claims 1-16 have been canceled.

Claims 17-29 have been newly added.

3. Newly submitted claim 29 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group I, claims 17-28, drawn to an isolated polynucléotide comprising a nucleotide sequence encoding a polypeptide having cycloartenol synthase activity, wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO:6 have at least 92% identity, a cell, transgenic plant and method comprising said polynucleotide, classified in class 800, subclass 298 for example.

Group II, claim 29, drawn to a method for isolating a polypeptide, classified in class 435, subclass 69.1, for example.

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the isolated polynucleotide can be used in a hybridization method for isolating other cycloartenol synthase polynucleotides.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the literature and sequence searches required for each of the Groups are not required for another of the Groups, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Applicant provisionally elected Group I (original claims 1-9) in the response filed 10/25/2005. Therefore, Group II, claim 29, is nonelected by original presentation and will not be considered in the instant office action.

4. Claims 17-28, including SEQ ID NO:6 are examined in the present office action.

Inventorship

5. In view of the papers filed 10/26/2005, the inventorship in this nonprovisional application has been changed by the deletion of Saverio Carl Falco, William D. Hitz, Brian McGonigle, Antony J. Rafalski and Omolayo O. Famodu.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Information Disclosure Statement

6. The information disclosure statement filed 6/1/2004 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because each publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, date, and place of publication. In the instant application, the NCBI accession numbers do not include an author and date. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 17 and 21-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims have been amended to recite "wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO:6 have at least 92% identity based on the Clustal alignment method" and the subject matter of all subsequent dependent claims. Applicants fail to point to support in the instant specification. Upon a cursory search of the specification, support could not be found. Applicants are required to point to support for the newly submitted claims filed 10/25/2005 or to amend the claims to delete the NEW MATTER.

Written Description

Claim Rejections - 35 USC § 112

8. Claims 17-18 and 21-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated polynucleotide comprising a nucleotide sequence encoding a polypeptide having cycloartenol synthase activity, wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO:6 have at least 92% or 95%

identity; a cell, transgenic plant, vector, chimeric gene, seed and method comprising said polynucleotide.

Applicants isolated their invention from a soybean cDNA library made from developing pods 6-7 mm long, and then comparing the isolated cDNA sequences to those sequences in known databases. In the instant case, the reference sequence is a cycloartenol synthase from *Glycyrrhiza glabra* (NCBI general identifier no. 4589852) (pages 17-20, Examples 1-2). Applicants disclose the soybean cycloartenol synthase cDNA clone, sdp2c.pk008.g6, is SEQ ID NO:5 encoding SEQ ID NO:6 (page 17, Table 2; page 4, Table 1).

The Applicants do not identify essential regions of the soybean cycloartenol synthase protein encoded by SEQ ID NO:5, nor do Applicants describe any polynucleotide sequences that encode a polypeptide exhibiting 92% sequence identity to SEQ ID NO:6 that encode a functional soybean cycloartenol synthase protein.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the

genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotide sequences encoding a cycloartenol synthase protein falling within the scope of the claimed genus of polynucleotides which encode a polypeptide exhibiting at least 92% sequence identity to SEQ ID NO:6 that encode a functional cycloartenol synthase protein. Applicants disclose SEQ ID NO:1 encoding SEQ ID NO:2, SEQ ID NO:3 encoding SEQ ID NO:4, SEQ ID NO:5 encoding SEQ ID NO:6, and SEQ ID NO:7 encoding SEQ ID NO:8 which are purported cycloartenol synthases from corn, rice, soybean, wheat and corn, respectively (page 4, Table 1), but Applicants have not indicated if the disclosed sequences encode complete proteins and Applicants have not presented an alignment of the proteins which indicates the conserved amino acids. It is not clear if the disclosed sequences are representative of the claimed genus because it is not indicated that the disclosed sequences encode proteins with cycloartenol synthase activity. In addition, Applicants have not disclosed a structure/function relationship for their claimed genus. Therefore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the soybean cycloartenol synthase protein, it remains unclear what features identify a soybean cycloartenol synthase protein. Since the genus of soybean cycloartenol synthase proteins has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Enablement

9. Claims 17-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to an isolated polynucleotide comprising a nucleotide sequence encoding a polypeptide having cycloartenol synthase activity, wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO:6 have at least 92% or 95% identity; a cell, transgenic plant, vector, chimeric gene, seed and method comprising said polynucleotide.

Applicants isolated their invention from a soybean cDNA library made from developing pods 6-7 mm long, and then comparing the isolated cDNA sequences to those sequences in known databases. In the instant case, the reference sequence is a cycloartenol synthase from *Glycyrrhiza glabra* (NCBI general identifier no. 4589852) (pages 17-20, Examples 1-2).

Applicants disclose the soybean cycloartenol synthase cDNA clone, sdp2c.pk008.g6, is SEQ ID NO:5 encoding SEQ ID NO:6 (page 17, Table 2; page 4, Table 1).

Applicants have not reduced to practice the invention. The specification fails to provide guidance for one of skill in the art how to make and/or use the claimed invention. Applicants have not transformed a wild-type plant with any of the claimed sequences to produce a plant with an increased sterol content. Applicants have only taught that the isolated nucleic acid sequence of SEQ ID NO:5 encodes SEQ ID NO:6 (page 17, Table 2; page 4, Table 1). Applicants have not taught how one skilled in the art can use the claimed sequences to generate a plant with an agronomically useful or important phenotype, without having to do additional undue experimentation in order to achieve the desired results. In addition, Applicants have not taught how one skilled in the art would use a plant transformed with any of the claimed sequences.

The state-of-the-art teaches overexpression of genes involved in sterol metabolism produce unexpected results. Lee et al (2004, Plant and Cell Physiology 45(8):976-984) report "there was no direct evidence for the regulatory function of squalene synthase (SS) gene in the biosynthesis of triterpene saponins. The regulation of the phytosterol and triterpene biosyntheses by overexpression of SS remains to be determined" (paragraph bridging pages 976-977). Lee et al disclose overexpression of Panax ginseng squalene synthase in adventitious roots of transgenic P. ginseng resulted in the up-regulation of all downstream genes tested, such as squalene epoxidase, beta-amyrin synthase and cycloartenol synthase, and that the squalene content decreased (pages 979-980).

The state-of-the-art is such that one of skill in the art cannot predict which nucleic acids that encode a polypeptide exhibiting 92% sequence identity to SEQ ID NO:6 will encode a

protein with the same activity as a protein encoded by SEQ ID NO:5. The prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited (Bowie et al, Science 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of tyrosine at position 410 (Tyr410) with threonine (Thr) converts cycloartenol synthase to an oxidosqualene cyclase, and abolishes cycloartenol formation (Herrera et al 2000, J. Am. Chem. Soc. 122:6765-6766, see especially page 6756, right column, 1st full paragraph; page 6766, left column, top paragraph).

Applicants have not disclosed how one makes or isolates any of the sequences that are encompassed by Applicants' broad claims. Applicants have not taught which regions of the respective polynucleotides can be used to amplify any of said polynucleotides or which regions can be used as a probe to isolate any of said polynucleotide sequences.

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:5 as probes or by designing primers to undisclosed regions of SEQ ID NO:6 and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed produce a phenotype that has not been disclosed by applicant.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claim 21 is rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

The claim recites "A cell comprising" which reads on a human being. Amending the claim to recite "An isolated cell" will obviate the rejection.

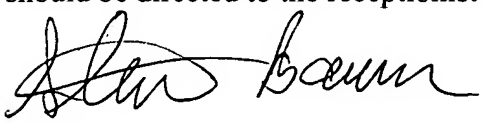
11. Claims 17-28 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated polynucleotide of SEQ ID NO:5 encoding SEQ ID NO:6, cell, transgenic plant, method, and vector comprising said polynucleotide.

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached at 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
November 28, 2005